Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

ACR Appropriateness Criteria® first trimester vaginal bleeding.

Bibliographic Source(s)

Brown DL, Packard A, Maturen KE, Deshmukh SP, Dudiak KM, Henrichsen TL, Meyer BJ, Poder L, Sadowski EA, Shipp TD, Simpson L, Weber TM, Zelop CM, Glanc P, Expert Panel on Womenâ€™s Imaging. ACR Appropriateness CriteriaÂ® first trimester vaginal bleeding. Reston (VA): American College of Radiology (ACR); 2017. 11 p. [82 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lane BF, Wong-You-Cheong JJ, Javitt MC, Glanc P, Brown DL, Dubinsky T, Harisinghani MG, Harris RD, Khati NJ, Mitchell DG, Pandharipande PV, Pannu HK, Podrasky AE, Shipp TD, Siegel CL, Simpson L, Wall DJ, Zelop CM, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® first trimester bleeding. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 7 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▯▯▯▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▯▯	Study Selection
▮▮▮▮▯	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▯▯▯	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▯	Evidence Summary Supporting Recommendations
▮▮▮▮▯	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▯▯▯▯	External Review
▮▮▮▯▯	Updating

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

First Trimester Vaginal Bleeding

Variant 1: First trimester vaginal bleeding. Positive urine or serum pregnancy test.

Procedure	Appropriateness Category	Relative Radiation Level
US pelvis transvaginal	Usually Appropriate	O
US pelvis transabdominal	Usually Appropriate	O
US duplex Doppler uterus	May Be Appropriate	O
MRI pelvis without IV contrast	May Be Appropriate	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢

Procedure	Appropriateness Category	Relative Radiation Level
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Ultrasound (US) is the primary imaging modality in the evaluation of patients presenting with vaginal bleeding in the first trimester of pregnancy. Magnetic resonance imaging (MRI) and computed tomography (CT) play a minor role in problem-solving the causes of bleeding but may be useful when US is severely limited, for an unusual ectopic pregnancy, or when uncommon diagnoses are suspected. US correlated with serum human chorionic gonadotrophin (hCG) levels and clinical presentation can usually differentiate causes of first-trimester bleeding. These include normal intrauterine pregnancy (IUP) with or without a subchorionic hematoma, nonviable IUP, gestational trophoblastic disease (GTD), and ectopic pregnancy, which can all present with vaginal bleeding. Bleeding in the first trimester occurs in 7% to 27% of pregnancies, with an overall risk of miscarriage of approximately 12%. US can usually differentiate an intrauterine from an ectopic pregnancy and a viable from a nonviable IUP. An overview of relevant US findings follows. Although it is important to diagnose ectopic pregnancies and nonviable IUPs, one should also guard against injury to normal pregnancies. Potential harm to a normal pregnancy can occur because of overinterpretation of a single US, misunderstanding the usefulness of the discriminatory level or serial values of hCG, and inappropriate treatment with methotrexate or dilation and curettage.

Variant 1: First Trimester Vaginal Bleeding. Positive Urine or Serum Pregnancy Test

US Transvaginal

Intrauterine Fluid Collection

The first visible US evidence of an IUP is a small spherical fluid collection with a hyperechoic rim, representing the gestational sac, located within the endometrium. Using high-frequency transvaginal transducers (generally about 7 MHz or higher), gestational sacs as small as 2 to 3 mm in mean sac diameter (MSD) may be visualized, corresponding to 4.5 to 5 weeks of gestation. Prior to the identification of a yolk sac or embryo in the gestational sac, the intradecidual sign may be helpful to confirm an IUP. The intradecidual sign consists of an intrauterine fluid collection with a hyperechoic rim located in the endometrium separate from the central echogenic line that represents the collapsed endometrial cavity. This sign, which can be visualized as early as 4.5 weeks, increases the probability of an IUP but is not reliable for diagnosing an IUP. It can be difficult to apply the intradecidual sign in some patients, as the central echogenic line is not always evident. The double decidual sac sign, typically defined as two echogenic rings around the intrauterine fluid collection, is another finding that seems to increase the likelihood of an IUP but is not a reliable sign and is of limited usefulness for confirming an IUP. The intradecidual sign and the double decidual sac sign both have poor interobserver agreement and neither is required for the diagnosis of an IUP.

Before a yolk sac or embryo is seen, there has been concern that fluid in the endometrial cavity, sometimes termed a pseudogestational sac, might be confused for a gestational sac. However, pseudogestational sacs can usually be recognized based on their shape (acute angle at the edge), contents (internal echoes), or location (in the endometrial cavity). If a nonspecific fluid collection in the uterus does not have the features of a pseudogestational sac, it should be interpreted as likely representing a gestational sac, and one should generally not undertake a treatment that could cause unintended harm to an IUP. Rarely, a decidual cyst could be mistaken for a gestational sac but usually does not have an echogenic rim and is usually not adjacent to the central echogenic line of the collapsed endometrial cavity.

The discriminatory level of hCG refers to the level at which a gestational sac should always be seen on transvaginal US in a normal singleton IUP and has historically been suggested as 1,000 to 2,000 mIU/mL. However, even a level of 2,000 mIU/mL has been found to be too low to exclude a normal IUP. If there is no transvaginal US evidence of a gestational sac when a single serum hCG is 3,000 mIU/mL or higher, it

is unlikely there will be a viable IUP. For a hemodynamically stable patient with no sonographic evidence of an IUP or ectopic pregnancy, management decisions should generally not be made based on a single hCG level. Follow-up hCG assay and US are usually appropriate in such a scenario.

Definitive Intrauterine Gestation

The yolk sac, a thin-walled, spherical structure with an anechoic center, is the first sonographic feature that confirms an IUP. It is usually visualized by transvaginal US in a gestational sac >8 mm in MSD]; however, in some normal pregnancies the gestational sac will be larger before a yolk sac is seen. The embryo will initially appear as a thickened, linear echogenic structure at the edge of the yolk sac. With transvaginal US, the embryo is usually seen by about 6 weeks gestational age and by the time the gestational sac grows to a MSD of 16 mm; however, in some normal pregnancies the gestational sac will be larger before an embryo is seen.

Although the absence of a yolk sac in a gestational sac >8 mm MSD or the absence of an embryo in a gestational sac >16 mm MSD is worrisome for a nonviable IUP, these cutoffs are not sufficient to make a definitive diagnosis of a nonviable IUP. Because of measurement variability and the desire to maximize diagnostic certainty and avoid inadvertent harm to a viable embryo, the MSD at which the absence of an embryo is diagnostic of a nonviable IUP is ≥25 mm with a technically adequate transvaginal US. However, only a minority of nonviable pregnancies will have a MSD of ≥25 mm. Thus, for smaller gestational sacs, time-based criteria for follow-up US may be useful. If the initial transvaginal US shows a MSD of <25 mm and a yolk sac without an embryo, a nonviable IUP can be diagnosed if there is no embryonic cardiac activity 11 or more days later. If the initial transvaginal US did not show a yolk sac in a gestational sac with a MSD of <25 mm, a nonviable IUP can be diagnosed if there is no embryonic cardiac activity 14 or more days later. It has been suggested that these time-based criteria to confirm nonviable pregnancies might be shortened in some patients, depending on gestational age and MSD at time of the initial US.

With transvaginal US, cardiac activity is normally evident in an embryo of any crown-rump length (CRL). Absence of cardiac activity in an embryo measuring ≥5 mm in CRL had previously been considered as diagnostic of embryonic demise. However, because of measurement variability and the desire to maximize diagnostic certainty and avoid inadvertent harm to a viable embryo, that CRL threshold has increased slightly to 7 mm. On transvaginal US, lack of embryonic cardiac activity in an embryo ≥7 mm in CRL confirms embryonic demise. Absence of cardiac activity in embryos <7 mm is still worrisome for embryonic demise, but the patient should generally be re-evaluated with a follow-up US in 7 to 10 days. Continued absence of embryonic cardiac activity on transvaginal US at least 7 days later confirms embryonic demise.

Once an IUP is definitely established by US, various US findings may be seen that are associated with a nonviable IUP. These include bradycardia, small gestational sac compared to embryo, enlarged amniotic cavity, empty amniotic cavity, absence of cardiac activity with visualization of the amnion, and abnormal size or shape of the yolk sac. However, these findings are not definitive for a nonviable IUP, and in these situations, follow-up US in correlation with serial quantitative serum beta hCG measurements is often useful. Subchorionic hematomas are not an infrequent finding during the first trimester. They are usually small and not thought to substantially increase the risk of a nonviable pregnancy. Large (two-thirds or more of the gestational sac circumference) subchorionic hematomas may be associated with an increased risk of nonviable pregnancy

Ectopic Pregnancy

Whenever an IUP is not identified in a patient with a positive pregnancy test, extrauterine locations for the pregnancy should be carefully evaluated. This involves identification of the ovaries and corpus luteum along with a careful search for any extraovarian mass that is not a paraovarian cyst or pedunculated fibroid because the vast majority of ectopic pregnancies are in the fallopian tube. Ectopic pregnancies are located ipsilateral to the corpus luteum in 70% to 80% of cases and it is important to distinguish between the corpus luteum and a tubal pregnancy in order to avoid misdiagnosis. The corpus luteum usually appears as a <3-cm cystic lesion with a thick wall (with or without internal echoes in the central cystic component, and with or without a crenulated appearance of the wall) or as a rounded hypoechoic lesion that may simulate a solid mass. The most important feature to assess is whether an identified

mass is inside the ovary or outside the ovary. Gentle pressure with the transvaginal transducer, and sometimes also with the examiner's hand on the lower anterior abdominal wall, may help demonstrate whether the mass and the ovary move together or separately, potentially distinguishing the intraovarian location of a corpus luteum from the extraovarian location of a tubal pregnancy.

Although visualization of an extrauterine gestational sac with a live embryo is 100% specific for an ectopic pregnancy, this situation is uncommon. More common, though slightly less specific, is an extrauterine mass with a fluid center and hyperechoic periphery, which has been termed a tubal ring. Additionally, the ectopic pregnancy may appear as a nonspecific heterogeneous mass with no identifiable gestational sac within it. This latter appearance has been reported as the most common sonographic finding of a tubal pregnancy. Even with such a nonspecific-appearing mass, tubal pregnancy is likely when the mass is outside the ovary (with no other obvious cause, such as a pedunculated fibroid or paraovarian cyst) in a patient with a positive serum hCG and no sonographic evidence of an IUP. Given the potential for inappropriate management with methotrexate or surgical intervention, the diagnosis of ectopic pregnancy should generally be based on positive findings and not solely on the absence of an IUP.

Assessment of any free intraperitoneal fluid is important in the evaluation for an ectopic pregnancy. In this setting, echoes within the free fluid are often due to blood. Trace anechoic free fluid in the pelvis is generally normal. The presence of more than a normal small amount of free fluid or echoes within the fluid, even without identification of an extraovarian mass, is concerning for an ectopic pregnancy. However, this finding is not specific and can also occur for other reasons, such as rupture of a hemorrhagic ovarian cyst with an early, nonvisualized IUP.

A minority of ectopic pregnancies occur in locations other than the fallopian tube. The most common nontubal locations are interstitial, cervical, and within a Cesarean section scar. Three-dimensional US may be useful if an interstitial pregnancy is suspected but the diagnosis is uncertain based on 2-D US. Rudimentary horn and abdominal pregnancies are less common, and ovarian ectopic pregnancy is rare. Coexisting intrauterine and extrauterine pregnancy (sometimes referred to as a heterotopic pregnancy) is rare, though is more likely to occur in women undergoing assisted reproduction techniques. In general, for a woman with a spontaneously occurring pregnancy, identification of an IUP excludes a coexisting ectopic pregnancy with near complete certainty. However, the adnexa should still be routinely evaluated.

Pregnancy of Unknown Location

"Pregnancy of unknown location" (PUL) is a transient state that refers to patients with a positive pregnancy test and no evidence of an ectopic pregnancy or an IUP on transvaginal US. Most patients with a PUL will have a nonviable IUP. Clinical findings of cramping pain and passage of tissue vaginally help support this diagnosis. If a prior pelvic US had demonstrated an IUP, an empty uterus on a follow-up US is definitive proof of a nonviable IUP that is no longer present. Following the diagnosis of a nonviable IUP, continued bleeding or persistent elevation or rise of serum hCG may suggest retained products of conception (RPOC). Grayscale and Doppler US are often helpful in this scenario. An endometrial mass, focal endometrial thickening, or marked diffuse thickening is suggestive of RPOC, particularly when flow is detected within the endometrial abnormality by Doppler imaging.

Other causes of PUL include an early IUP (<4.5-5 weeks) or a nonvisualized ectopic pregnancy. A small minority of patients with PUL (probably about 7%-20% but likely more toward the lower end of that range), will later be diagnosed with an ectopic pregnancy. Patients with a PUL can pose a diagnostic challenge. If the patient is hemodynamically stable, follow-up hCG and/or US should generally be performed before surgical or medical therapy is undertaken, regardless of the initial hCG level.

Gestational Trophoblastic Disease

When US does not show an intrauterine gestational sac, but rather a hyperechoic area in the endometrium with multiple cystic spaces, one should consider a complete molar pregnancy, the most common form of GTD. In the earlier part of the first trimester, this classic appearance may be absent and the sonographic findings more variable. Complete molar pregnancy can sometimes appear similar to RPOC. Partial molar pregnancy can be more difficult to diagnose sonographically than complete molar

pregnancy but should be considered if an embryo is present with cystic change in the early placenta. The US findings of partial molar pregnancy overlap those of a nonviable IUP with hydropic degeneration of the early placenta. The hCG is often, but not always, inappropriately elevated with GTD. Definitive diagnosis is based on histopathological evaluation of uterine contents.

US Transabdominal

Most research studies have used transvaginal US, and there is little evidence in regards to diagnosis of nonviable IUP with transabdominal US alone. Transabdominal US may be adequate in some patients if the diagnosis is clear, such as when a viable IUP and normal adnexa are demonstrated in a patient with no risk factors for heterotopic pregnancy. Transabdominal US is more likely to be adequate later in the first trimester as opposed to the early first trimester.

Ectopic Pregnancy

If an abnormal amount of free intraperitoneal fluid is identified in the pelvis, transabdominal US should be used to evaluate the flanks and dependent locations in the right upper (Morison pouch) and left upper quadrants. It is difficult to reliably predict tubal rupture by US. Larger amounts of free intraperitoneal fluid correlate with ruptured ectopic pregnancy, but in about one-third of cases with a large amount of free intraperitoneal fluid, the fallopian tubes are intact. Clotted blood in the pelvis can sometimes be mistaken for mesentery or blend in with adjacent organs such as the uterus and be difficult to recognize.

US Duplex Doppler

When a normal or potentially normal IUP is present, pulsed Doppler US (whether spectral, color, or power Doppler) of the pregnancy should generally be avoided in the first trimester due to concerns about potential bioeffects in the developing embryo. Documentation of embryonic cardiac activity is best done with M-mode US as the heart rate can be measured. Video clips can also be used to document embryonic cardiac activity.

Once a normal IUP has been excluded, Doppler US may be useful when other diagnoses such as RPOC are suspected. Doppler US is not generally needed to make a diagnosis of GTD, but may be helpful as an ancillary tool in the management of some patients with GTD. Doppler US is rarely useful for diagnosing tubal pregnancies as both the corpus luteum and a tubal pregnancy often have flow detected peripherally. Although Doppler US could conceivably be useful in some nontubal ectopic pregnancies such as cervical, interstitial, or Cesarean section scar pregnancies, its diagnostic utility for these diagnoses has not been well established in the literature.

Miscellaneous Diagnoses

US can also depict some unusual causes of first-trimester bleeding, such as what traditionally has been termed a uterine arteriovenous malformation (AVM). The terminology of this entity is evolving as many of these are not true AVMs and will resolve spontaneously. Other terms such as "vascular lesions" and "enhanced myometrial vascularity" have been proposed. Although suggestive findings may be seen on grayscale US, Doppler imaging is important for making the diagnosis of an AVM. True AVMs are usually acquired and due to prior uterine instrumentation. One should be cautious when diagnosing an AVM/enhanced myometrial vascularity in the postpartum period, as similar US findings can occur with RPOC and with GTD. Low-resistance arterial flow in the myometrium may also be due to subinvolution of the placental bed. Although usually seen in the postpartum period, subinvolution of the placental bed can also occur after a nonviable IUP in the first trimester and simulate an AVM. Many of these vascular lesions will respond to conservative management; velocity in the suspected vascular lesion may be helpful in guiding management. In stable patients, follow-up US should be considered before diagnosing or treating a potential AVM.

MRI

While an early pregnancy may be recognized on MRI, it generally is due to unintentional imaging of the pregnancy. MRI is rarely needed for evaluating an IUP or tubal pregnancy. However, one may occasionally

recognize tubal pregnancies on MRI, and MRI may be helpful as a problem-solving tool for nontubal ectopic pregnancies or GTD. MRI may also help in cases of unusual implantation sites or in women with uterine anomalies. In pregnancy, gadolinium should be used with caution and only when critical and the potential benefits are felt to be justified. Gadolinium is not generally recommended in a normal first-trimester pregnancy. MRI without gadolinium is thought to be safe in the first trimester of pregnancy.

RPOC may be identified by MRI, but MRI has little role in making the diagnosis of RPOC. RPOC and GTD may both manifest as an enhancing endometrial mass but are usually distinguishable on clinical grounds. Contrast-enhanced pelvic MRI may be helpful to evaluate the extent of myometrial invasion and local extrauterine spread of GTD. Uterine AVM can also be diagnosed with MRI.

CT

An early IUP may be recognized on CT, but it is usually due to unintentional imaging of the pregnancy. Because of its ionizing radiation, CT is generally not performed to evaluate vaginal bleeding in the first trimester of pregnancy. CT may identify an ectopic pregnancy, but reported cases of ectopic pregnancy diagnosed on CT were often performed for other reasons or in patients not known to be pregnant. When a patient is clinically unstable, emergent care should generally not be delayed by additional imaging with CT or MRI. RPOC may be identified by CT, particularly when an enhancing mass is seen, but CT has little role in making the diagnosis of RPOC and the findings overlap those of GTD. In patients with GTD, CT may be helpful in evaluating the extent of extrauterine spread.

Summary of Recommendations

Transvaginal and transabdominal US are the most appropriate imaging modalities in patients with abnormal vaginal bleeding in the first trimester of pregnancy. Transvaginal US is generally the preferred modality. Transabdominal US is often complementary to transvaginal US and may sometimes be adequate alone.

Safety Considerations in Pregnant Patients

Imaging of the pregnant patient can be challenging, particularly with respect to minimizing radiation exposure and risk. For further information and guidance, see the following ACR documents:

ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation
ACR-ACOG-AIUM Practice Guideline for the Performance of Obstetrical Ultrasound
ACR Guidance Document for Safe MR Practices
ACR Manual on Contrast Media

Abbreviations

CT, computed tomography
IV, intravenous
MRI, magnetic resonance imaging
US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

First trimester vaginal bleeding

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Obstetrics and Gynecology

Radiology

Intended Users

Advanced Practice Nurses

Health Care Providers

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging procedures in patients with first trimester vaginal bleeding

Target Population

Pregnant women with first trimester vaginal bleeding

Interventions and Practices Considered

1. Ultrasound (US)
    - Pelvis transvaginal
    - Pelvis transabdominal
    - Duplex Doppler uterus
2. Magnetic resonance imaging (MRI), pelvis
    - Without intravenous (IV) contrast
    - Without and with IV contrast
3. Computed tomography (CT), pelvis
    - Without IV contrast
    - With IV contrast
    - Without and with IV contrast

Major Outcomes Considered

- Utility of imaging procedures in diagnosis and evaluation of first trimester vaginal bleeding
- Sensitivity and specificity of imaging procedures in diagnosis and evaluation of first trimester vaginal bleeding

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Of the 55 citations in the original bibliography, 33 were retained in the final document.

A literature search was conducted in September 2016, October 2016 and June 2017 to identify additional evidence published since the *ACR Appropriateness Criteria® First Trimester Vaginal Bleeding* topic was finalized. Using the search strategies described above, 382 unique articles were found. 18 articles were added to the bibliography. The remaining articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, or the results were unclear or biased.

The author added 27 citations from bibliographies, Web sites, or books that were not found in the literature searches, including 16 articles outside of the search date ranges.

Four citations are supporting documents that were added by staff.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 55 citations in the original bibliography, 33 were retained in the final document. The literature search conducted in September 2016, October 2016, and June 2017 found 18 articles that were added to the bibliography. The author added 27 citations from bibliographies, Web sites, or books that were not

found in the literature searches, including 16 articles outside of the search date ranges. Four citations are supporting documents that were added by staff.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Overview

The purpose of the rating rounds is to systematically and transparently determine the panels' recommendations while mitigating any undue influence of one or more panel members on another individual panel members' interpretation of the evidence. The panel member's rating is determined by reviewing the evidence presented in the Summary of Literature Review and assessing the risks or harms of performing the procedure or treatment balanced with the benefits of performing the procedure or treatment. The individual panel member ratings are used to calculate the median rating, which determines the panel's rating. The assessment of the amount of deviation of individual ratings from the panel rating determines whether there is disagreement among the panel about the rating.

The process used in the rating rounds is a modified Delphi method based on the methodology described in the RAND/UCLA Appropriateness Method User Manual.

The appropriateness is rated on an ordinal scale that uses integers from 1 to 9 grouped into three categories (see the "Rating Scheme for the Strength of the Recommendations" field).

Determining the Panel's Recommendation

> Ratings represent an individual's assessment of the risks and benefits of performing a specific procedure for a specific clinical scenario on an ordinal scale. The recommendation is the appropriateness category (i.e., "Usually appropriate", "May be appropriate", or "Usually not appropriate").
>
> The appropriateness category for a procedure and clinical scenario is determined by the panel's median rating without disagreement (see below for definition of disagreement). The panel's median rating is calculated after each rating round. If there is disagreement after the second rating round, the rating category is "May be appropriate (Disagreement)" with a rating of "5" so users understand the group disagreed on the final recommendation. The actual panel median rating is documented to provide additional context.
>
> Disagreement is defined as excessive dispersion of the individual ratings from the group (in this case, an Appropriateness Criteria [AC] panel) median as determined by comparison of the interpercentile range (IPR) and the interpercentile range adjusted for symmetry (IPRAS). In those instances when the IPR is greater than the IPRAS, there is disagreement. For a complete discussion, please refer to chapter 8 of the RAND/UCLA Appropriateness Method User Manual.
>
> Once the final recommendations have been determined, the panel reviews the document. If two thirds of the panel feel a final recommendation is wrong (e.g., does not accurately reflect the evidence, may negatively impact patient health, has unintended consequences that may harm health care, etc.) and the process must be started again from the beginning.

For additional information on the ratings process see the Rating Round Information document (see the "Availability of Companion Documents" field).

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 82 references cited in the *ACR Appropriateness Criteria® First Trimester Vaginal Bleeding* document, 1 is categorized as a therapeutic reference that may have design limitations. Additionally, 79 references are categorized as diagnostic references including 6 good-quality studies and 19 quality studies that may have design limitations. There are 54 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

Although there are references that report on studies with design limitations, 6 good-quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Ultrasound (US) correlated with serum human chorionic gonadotrophin (hCG) levels and clinical presentation can usually differentiate causes of first-trimester bleeding.
- US can usually differentiate an intrauterine from an ectopic pregnancy and a viable from a nonviable intrauterine pregnancy (IUP).

Potential Harms

- Although it is important to diagnose ectopic pregnancies and nonviable intrauterine pregnancies (IUPs), one should also guard against injury to normal pregnancies. Potential harms to a normal pregnancy can occur because of overinterpretation of a single US, misunderstanding the usefulness of the discriminatory level or serial values of human chorionic gonadotrophin (hCG), and inappropriate treatment with methotrexate or dilation and curettage.
- In pregnancy, gadolinium should be used with caution and only when critical and the potential benefits are felt to be justified.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Contraindications

Contraindications

- When a normal or potentially normal intrauterine pregnancy (IUP) is present, pulsed Doppler ultrasound (US) (whether spectral, color, or power Doppler) of the pregnancy should generally be avoided in the first trimester due to concerns about potential bioeffects in the developing embryo.
- Gadolinium is not generally recommended in a normal first-trimester pregnancy.

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used

for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Brown DL, Packard A, Maturen KE, Deshmukh SP, Dudiak KM, Henrichsen TL, Meyer BJ, Poder L, Sadowski EA, Shipp TD, Simpson L, Weber TM, Zelop CM, Glanc P, Expert Panel on Womenâ€™s Imaging. ACR Appropriateness CriteriaÂ® first trimester vaginal bleeding. Reston (VA): American College of Radiology (ACR); 2017. 11 p. [82 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The funding for the process is assumed entirely by the American College of Radiology (ACR). ACR staff support the expert panels through the conduct of literature searches, acquisition of scientific articles, drafting of evidence tables, dissemination of materials for the Delphi process, collation of results, conference calls, document processing, and general assistance to the panelists.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging

Composition of Group That Authored the Guideline

Panel Members: Douglas L. Brown, MD (*Principal Author*); Ann Packard, MD (*Research Author*); Katherine E. Maturen, MD, MS (*Panel Chair*); Sandeep Prakash Deshmukh, MD; Kika M. Dudiak, MD; Tara L. Henrichsen, MD; Benjamin J. Meyer, MD; Liina Poder, MD; Elizabeth A. Sadowski, MD; Thomas D. Shipp, MD, RDMS; Lynn Simpson, MD; Therese M. Weber, MD; Carolyn M. Zelop, MD; Phyllis Glanc, MD (*Specialty Chair*)

Financial Disclosures/Conflicts of Interest

Disclosing Potential Conflicts of Interest and Management of Conflicts of Interest

An important aspect of committee operations is the disclosure and management of potential conflicts of interest. In 2016, the American College of Radiology (ACR) began an organization-wide review of its conflict of interest (COI) policies. The current ACR COI policy is available on its Web site. The Appropriateness Criteria (AC) program's COI process varies from the organization's current policy to accommodate the requirements for qualified provider-led entities as designated by the Centers for Medicare and Medicaid Services' Appropriate Use Criteria (AUC) program.

When physicians become participants in the AC program, welcome letters are sent to inform them of their panel roles and responsibilities, including a link to complete the COI form. The COI form requires disclosure of all potential conflicts of interest. ACR staff oversees the COI evaluation process, coordinating with review panels consisting of ACR staff and members, who determine when there is a conflict of interest and what action, if any, is appropriate. In addition to making the information publicly available, management may include exclusion from some topic processes, exclusion from a topic, or exclusion from the panel.

Besides potential COI disclosure, AC staff begins every committee call with the conflict of interest disclosure statement on the Web site reminding members to update their COI forms. If any updates to their COI information have not been submitted, they are instructed not to participate in discussion where an undisclosed conflict may exist.

Finally, all ACR AC are published as part of the Journal of the American College of Radiology (JACR) electronic supplement. Those who participated on the document and are listed as authors must complete the JACR process that includes completing the International Committee of Medical Journal Editors (ICMJE) COI form which is reviewed by the journal's staff/publisher.

The authors have no conflicts of interest related to the material discussed in this article.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lane BF, Wong-You-Cheong JJ, Javitt MC, Glanc P, Brown DL, Dubinsky T, Harisinghani MG, Harris RD, Khati NJ, Mitchell DG, Pandharipande PV, Pannu HK, Podrasky AE, Shipp TD, Siegel CL, Simpson L, Wall DJ, Zelop CM, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® first trimester bleeding. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 7 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2017. Available from the American College of Radiology (ACR) Web site .

ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2017 Sep. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2018. 4 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2017. 125 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2017 Mar. 4 p. Available from the ACR Web site .

ACR Appropriateness Criteria® first trimester vaginal bleeding. Evidence table. Reston (VA): American College of Radiology; 2017. 29 p. Available from the ACR Web site .

ACR Appropriateness Criteria® first trimester vaginal bleeding. Literature search summary. Reston (VA): American College of Radiology; 2017. 3 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on February 10, 2006. The guideline developer agreed to not review the content. This NGC summary was updated by ECRI Institute on June 16, 2010. The guideline developer agreed to not review the content. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast

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